

5 Claims

1. A transgenic non-human animal whose genome comprises a polynucleotide encoding human ICAM-1 domains D1 and D2.

10 2. A transgenic non-human animal according to claim 1, wherein said polynucleotide encodes human ICAM-1 domains D1 and D2 and one or more host non-human animal ICAM-1 domains D3, D4 or D5.

15 3. A transgenic non-human animal according to claim 2, wherein said polynucleotide encodes human ICAM-1 domains D1 and D2 and host non-human animal ICAM-1 domains D3, D4 and D5.

20 4. A transgenic non-human animal according to any of claims 1 to 3, wherein said polynucleotide comprises one or more of the following polynucleotide sequences:

(a) a polynucleotide sequence having at least 90%, more preferably 95%, 96%, 97%, 98%, 99% or 100% identity to the polynucleotide sequence of SEQ ID No:2;

25 (b) a polynucleotide sequence having at least 90%, more preferably 95%, 96%, 97%, 98%, 99% or 100% identity to the polynucleotide sequence of SEQ ID No:3;

(c) a polynucleotide sequence encoding a polypeptide sequence having at least 90%, more preferably 95%, 96%, 97%, 98%, 99% or 100% identity to the polypeptide sequence of SEQ ID No:5;

30 (d) a polynucleotide sequence encoding a polypeptide sequence having at least 90%, more preferably 95%, 96%, 97%, 98%, 99% or 100% identity to the polypeptide sequence of SEQ ID No:6;

(e) a polynucleotide fragment of SEQ ID No:1 (or a sequence with at least 90%, or more preferably 95%, 96%, 97%, 98%, 99% or 100% identity to it) encoding human ICAM-1 domains D1 and D2; and

35 (f) a polynucleotide sequence encoding a polypeptide fragment of SEQ ID No:4 (or a sequence with at least 90%, more preferably 95%, 96%, 97%, 98%, 99% or 100% identity to it) comprising human ICAM-1 domains D1 and D2.

40 5. A transgenic non-human animal according to any of claims 1 to 4, whose genome further comprises a regulatory sequence capable of directing expression of said polynucleotide in cells and/or tissues of the respiratory tract.

- 5 6. A transgenic non-human animal according to claim 5, wherein said regulatory sequence is a promoter selected from the group consisting of CMV, SV40, human surfactant protein C (SPC) or Clara cell 10KDa secretory (CC10).
- 10 7. A transgenic non-human animal according to any one of claims 1 to 4, which expresses an ICAM-1 polypeptide comprising human ICAM-1 domains D1 and D2.
- 15 8. A transgenic non-human animal according to claim 7, which expresses a chimaeric ICAM-1 polypeptide comprising human ICAM-1 domains D1 and D2.
- 20 9. A transgenic non-human animal according to claim 8, which expresses a chimaeric ICAM-1 polypeptide comprising one or more of the following polypeptide sequences:
- 25 (a) a polypeptide fragment of SEQ ID No:4 (or a sequence with at least 90%, more preferably 95%, 96%, 97%, 98%, 99% or 100% identity to it) comprising human ICAM-1 domains D1 and D2;
- (b) a polypeptide sequence having at least 90%, more preferably 95%, 96%, 97%, 98%, 99% or 100% identity with the polypeptide sequence of SEQ ID No:5; and
- (c) a polypeptide sequence having at least 90%, more preferably 95%, 96%, 97%, 98%, 99% or 100% identity with the polypeptide sequence of SEQ ID No:6.
- 30 10. A transgenic non-human animal according to claim 9, wherein said chimaeric ICAM-1 polypeptide comprises one or more of host non-human animal ICAM-1 domains D3, D4 and D5.
- 35 11. A transgenic non-human animal according to claim 10, wherein said chimaeric ICAM-1 polypeptide comprises host non-human animal ICAM-1 domains D3, D4, and D5.
- 40 12. A transgenic non-human animal according to any of claims 9 to 11, wherein said chimaeric ICAM-1 polypeptide is expressed in the cells and/or tissues of the respiratory tract.
- 45 13. A transgenic non-human animal according to any of claims 8 to 12, wherein said chimaeric ICAM-1 polypeptide is capable of binding and supporting major group HRV infection.

- 5 14. A transgenic non-human animal according to any preceding claim, wherein
said animal is a rodent.
- 10 15. A transgenic non-human animal according to any preceding claim, wherein
said animal is a mouse or a rat.
- 15 16. A transgenic non-human animal according to claim 15, wherein said animal is
a mouse.
- 20 17. A transgenic animal according to any of claims 1 to 6, wherein said animal is
a mouse and said polynucleotide comprises one or more of the following
polynucleotide sequences:
- 25 (a) a polynucleotide sequence having at least 90%, more preferably 95%,
96%, 97%, 98%, 99% or 100% identity to the polynucleotide
sequence of SEQ ID No:8;
- 30 (b) a polynucleotide sequence having at least 90%, more preferably 95%,
96%, 97%, 98%, 99% or 100% identity to the polynucleotide
sequence of SEQ ID No:9;
- 35 (c) a polynucleotide sequence having at least 90%, more preferably
95%, 96%, 97%, 98%, 99%, or 100% identity to the polynucleotide
sequence of SEQ ID No:10;
- 40 (d) a polynucleotide sequence encoding a polypeptide sequence having
at least 90%, more preferably 95%, 96%, 97%, 98%, 99% or 100%
identity to the polypeptide sequence of SEQ ID No:11;
- 45 (e) a polynucleotide sequence encoding a polypeptide sequence having
at least 90% or more preferably 95%, 96%, 97%, 98%, 99% or 100%
identity to the polypeptide sequence of SEQ ID No:12;
- 50 (f) A polypeptide sequence encoding a polypeptide sequence having at
least 90%, more preferably 95%, 96%, 97%, 98%, 99%, or 100%
identity to the polypeptide sequence of SEQ ID No:13;
- 55 (g) a polynucleotide fragment of SEQ ID No:7 (or a sequence with at least
90%, more preferably 95%, 96%, 97%, 98%, 99% or 100% identity to
it) encoding one or more of murine ICAM-1 domains D3, D4 and D5;
- 60 (h) a polynucleotide sequence having at least 90%, more preferably 95%,
96%, 97%, 98%, 99% or 100% identity to the polynucleotide
sequence of SEQ ID No:14; and
- 65 (i) a polynucleotide encoding a polypeptide having at least 90%, more
preferably 95%, 96%, 97%, 98%, 99% or 100% identity to the
polypeptide sequence of SEQ ID No:15.

- 5 18. A transgenic animal according to any of claims 7 to 13, wherein said animal is
a mouse and said chimaeric ICAM-1 polypeptide comprises one or more of
the following polypeptide sequences:
- 10 (a) a polypeptide fragment of SEQ ID No:7 (or a sequence with at least
90%, more preferably 95%, 96%, 97%, 98%, 99% or 100% identity to
it) comprising one or more of murine ICAM-1 domains D3, D4 and D5;
- 15 (b) a polypeptide sequence having at least 90%, more preferably 95%,
96%, 97%, 98%, 99% or 100% identity with the polypeptide sequence
of SEQ ID No:11;
- 20 (c) a polypeptide sequence having at least 90%, more preferably 95%,
96%, 97%, 98%, 99% or 100% identity with the polypeptide sequence
of SEQ ID No:12;
- 25 (d) a polypeptide sequence having at least 90%, more preferably 95%,
96%, 97%, 98%, 99% or 100% identity with the polypeptide sequence
of SEQ ID No:13; and
- 30 (e) a polypeptide sequence having at least 90%, more preferably 95%,
96%, 97%, 98%, 99% or 100% identity to the polypeptide sequence of
SEQ ID No:15.
- 25 19. A chimaeric transgene comprising a polynucleotide encoding human ICAM-1
domains D1 and D2.
- 30 20. A chimaeric transgene according to claim 19, wherein said polynucleotide
encodes one or more of host non-human animal ICAM-1 domains D3, D4 and
D5.
- 35 21. A chimaeric transgene according to claim 20, wherein said polynucleotide
encodes host non-human animal ICAM-1 domains D3, D4 and D5.
- 40 22. A chimaeric transgene according to any of claims 19 to 22, wherein said host
non-human animal is a rodent, preferably a mouse.
- 45 23. A chimaeric transgene according to any of claims 19 to 22, further comprising
a regulatory sequence capable of directing expression of said polynucleotide
in cells and/or tissues of the respiratory tract.
24. A vector comprising the transgene according to any of claims 19 to 23.
- 45 25. A cell stably transfected or transformed with the transgene according to any
of claims 19 to 23.

- 5 26. A method of producing the transgenic non-human animal of any of claims 1 to
18.
- 10 27. A method according to claim 26, wherein the transgene according to any of
claims 19 to 23 is introduced into non-human animal ES cells using
electroporation, retroviral vectors or lipofection for gene transfer.
- 15 28. A method according to claim 27, wherein the non-human transgenic animal is
a mouse and the transgene is introduced into mouse ES cells using
electroporation, retroviral vectors or lipofection for gene transfer, particularly
electroporation.
- 20 29. A method of screening test agents for use in the treatment of a condition
associated with or exacerbated by major group HRV infection, the method
comprising administering a test agent to a transgenic non-human animal as
defined in any one of claims 1 to 18, and determining whether the test
substance (i) prevents or delays the onset of the condition or (ii) treats or
alleviates the condition.